Paludisme : A propos d'un cas autochtone en Tunisie
Malaria: An indigenous case in Tunisia

Amdouni. R [1,2], Ben Ahmed. S [1,2], Farhat. R [1,2], Haddad. S [1,2], Rhayem. S [1,2], Zarrouk. H [1,3], Jouini. H [1,3], Kallel. A [1,4], Cheikhrouhou. S [1,4], Khemiri. M [1,2]

[1] Université de Tunis El Manar, Faculté de Médecine de Tunis, 1007, Tunis, Tunisie
[2] Hôpital d'enfants Béchir Hamza, service de pédiatrie A, 1007, Tunis, Tunisie
[3] Hôpital d'enfants Béchir Hamza, service d'hématologie biologique, 1007, Tunis, Tunisie
[4] Hôpital la Rabta, laboratoire de parasitologie, 1007, Tunis, Tunisie

RESUME

Introduction : Le paludisme, éradiqué en Tunisie depuis 1979, représente toujours une menace potentielle de résurgence compte tenu de la persistance de l'anophélisme local.

Objectif : Décrire les caractéristiques cliniques et épidémiologiques d'un cas présumé de paludisme autochtone à Plasmodium falciparum identifié en juin 2023.

Méthodes : Il s'agit d'un rapport de cas clinique avec analyse épidémiologique d'un cas de paludisme sévère diagnostiqué au service de pédiatrie A de l'Hôpital des Enfants de Tunis en juillet 2023.

Résultats : Un enfant de 30 mois de sexe masculin a été admis pour exploration d'une fièvre prolongée associée à des signes digestifs. L'examen physique a révélé : fièvre avec agitation, polypnée, tachycardie sans signes d'hypoperfusion périphérique, et hépatosplénomégalie. La biologie a montré une leuco-thrombopénie avec syndrome inflammatoire biologique. Le diagnostic de paludisme a été initialement suggéré par un frottis sanguin puis confirmé par test rapide et goutte épaisse, avec une parasitémie de 6 %. Compte tenu de la présence de critères de gravité, le traitement a été initié en unité de soins intensifs avec une évolution clinico-biologique favorable. Les investigations entomologiques et épidémiologiques ont conclu à un cas probablement autochtone.

Conclusion : La survenue d'un cas de paludisme autochtone impose des mesures de prévention strictes ainsi que la mise en place d'un système de surveillance épidémiologique.

Mots clés : Plasmodium falciparum, paludisme autochtone, enfant, Tunisie

ABSTRACT

Background: Malaria, eradicated in Tunisia since 1979, still presents a potential threat of resurgence given the persistence of local anophelitism.

Aim: Describe the clinical and epidemiological characteristics of A presumed indigenous P. falciparum malaria case was identified in June 2023.

Methods: This is a clinical case report with an epidemiological analysis of a severe malaria case diagnosed at the Pediatrics Department A of the Children's Hospital of Tunis in July 2023.

Results : A 30-month-old male child was admitted for a prolonged febrile inness with gastrointestinal symptoms. The physical examination revealed fever with agitation, polypnea, tachycardia without signs of peripheral hypoperfusion, and hepatosplenomegaly. Leuko-thrombocytopenia with a biological inflammatory syndrome were found in biology. Malaria diagnosis was initially suggested on a blood smear then confirmed by rapid test and thick smear with parasitemia at 6%. Given the presence of severe criteria, treatment was initiated in the intensive care unit with a favorable clinical-biological evolution. Entomological and epidemiological investigations concluded a probable indigenous case.

Conclusion : The presence of an indigenous Malaria case enforces drastic prevention measures as well as the establishment of an epidemiological surveillance system.

Keywords: Plasmodium Falciparum, autochthonous malaria, children, Tunisia

Corresponding author:
Dr Amdouni Rim
E-mail : rym.amdouni@hotmail.com / rim.amdouni@fmt.utm.tn
Téléphone : +216 27 158 895
Nombre de mots : 2207

BACKGROUND

Malaria is a deadly parasitic disease that is widespread throughout the world. In 2023, the World Health Organization (WHO) estimated that 263 million people were affected, resulting in approximately 597,000 deaths (1). This disease was once endemic and caused significant morbidity in Tunisia in an endemic-epidemic form (1). However, thanks to the implementation of the national malaria eradication program, in particular the intensive control campaigns carried out between 1968 and 1972 with the active collaboration of the WHO, Tunisia recorded a significant turning point (1,2). Since 1979, the year that marked the eradication of the last indigenous case, the country has succeeded in stopping the active transmission of this parasitosis on its territory through the elimination of malaria vectors, the improvement of housing conditions, and raising public awareness of preventive measures (2,3).

The currently recorded cases are imported ones, often linked to international travel, as well as some post-transfusion cases and rare cases of airport malaria (2,4). Yet, Tunisia remains, like other nations harboring the vector, vulnerable to the potential threat of an upsurge (5).

Here in, we reported a malaria case, identified in Tunisia in July 2023, whose presentation supports the hypothesis of an indigenous case. We aimed to detail the clinical and epidemiological characteristics of the case by analyzing the different possible modes of transmission.

METHODS

This is a clinical observation report with epidemiological analysis of a severe malaria case diagnosed in July 2023 in the Pediatrics department 'A' of the children's hospital of Tunis. Malaria was suspected on a blood smear in the setting of prolonged fever and confirmed by thick blood film examination.

The epidemiological investigation included:

1- Parental interview: to determine residence, recent travel, blood exposure, and contact with persons from endemic areas.

2- Multidisciplinary discussion: among clinicians, biologists, and epidemiologists.

3- Entomological survey: conducted in regions visited by the family (Ariana, Tabarka, Bizerte, and around Tunis-Carthage airport)

The diagnosis of severe malaria was established according to the (WHO criteria. A case was classified as severe in the presence of one or more of the following findings [1]: Impaired consciousness or prostration, multiple convulsions, severe anemia (hemoglobin <7 g/dL), hypoglycemia (<2.2 mmol/L or 40 mg/dL), acidosis or respiratory distress, hemoglobinuria or acute renal impairment, jaundice with evidence of organ dysfunction, pulmonary edema or acute respiratory distress syndrome (ARDS), significant bleeding or disseminated intravascular coagulation, shock or hypotension, high parasitemia (≥4–5% infected red blood cells).

In this case, severity was defined by the presence of respiratory distress, severe anemia, and a parasitemia level of 6%, fulfilling WHO criteria for severe *Plasmodium falciparum* malaria.

CASE PRESENTATION

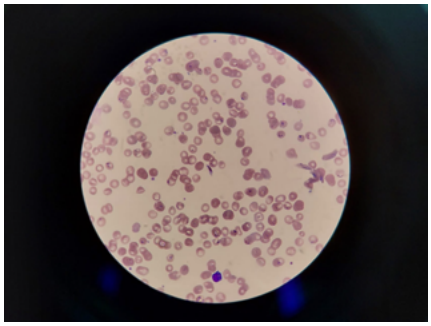
A boy, aged 30 months, was admitted in July 2023 for prolonged fever lasting 15 days accompanied by digestive signs of diarrhea and vomiting. The clinical examination found a pale patient with an altered general condition. The patient was polypneic at 50 cpm with free lung auscultation and normal oxygen saturation, tachycardic at 120 bpm with normal blood pressure. The patient had hepatosplenomegaly without peripheral lymphadenopathy. During his hospitalization, the patient had recurrent attacks of chills and fever. The blood count revealed a tendency to leukopenia with a white blood cell count of 4500/mm3 with bicytopenia made up of a normochromic normocytic regenerative anemia (Hemoglobin=5.8g/dl) (NV: 11 to 15g/dl) with a negative direct Coombs test and a thrombocytopenia at 79,000/mm3 (NV: 150,000 to 450,000/mm3). C- Reactive Protein was 65 mg/l (NV <2mg/l), serum ferritin was elevated at 885 ng/L (NV: 30 to 400 ng/l) as well as lactate dehydrogenase level at 606 U/L (NV: 135 to 225 U/L) and triglycerides at 6.7 mmol/L (NV<1,7mmol) (table 1).

Table 1 : Hematological and biochemical parameters

Laboratory Parameter	Patient Value	Normal Range (NR)
White blood cells (WBC)	4,500 /mm³	4,000 – 10,000 /mm³
Hemoglobin (Hb)	5.8 g/dL	11 – 15 g/dL
Anemia	Normochromic normocytic, regenerative	–
Direct Coombs test	Negative	Negative
Platelets (PLT)	79,000 /mm³	150,000 – 450,000 /mm³
C-Reactive Protein (CRP)	65 mg/L	< 2 mg/L
Serum ferritin	885 ng/mL	30 – 400 ng/mL
Lactate dehydrogenase (LDH)	606 U/L	135 – 225 U/L
Triglycerides	6.7 mmol/L	< 1.7 mmol/L
Parasitemia (*Plasmodium falciparum*)	6 %	N/A

Hemolysis markers, bilirubin levels, and renal function were assessed and found to be within normal limits. The first-line infectious investigation, including series of blood cultures, a cytobacteriological examination of urine, a chest x-ray as well as stool cultures, was negative. Plasmodium Falciparum was identified on a blood smear given the high parasitemia (figure 1).

Figure 1 : This blood smear shows red blood cells infected with crescent-shaped Plasmodium falciparum gametocytes, indicating an active malaria infection



The diagnosis of malaria was confirmed by a positive rapid test and thick blood film. The clinical form was considered severe given a high parasitemia of 6%, respiratory signs and hematological anomalies. The child was transferred to an intensive care unit for 48 hours with non-invasive ventilatory support. Anti-malaria treatment was started immediately with artesunate intravenously for five days followed by a relay with arthemeter lumefantrine orally for three days. At Day 14, the patient was clinically asymptomatic, and both blood smear and thick film were negative for Plasmodium parasites. At Day 28, the patient remained clinically stable with persistently negative parasitological findings, confirming sustained recovery.

- The epidemiological investigation revealed that the child:

1. Lives with his parents in Jardins d'El Menzah in the governorate of Ariana, 9km from Tunis Carthage airport.
2. Had no history of transfusion or accident involving exposure to blood.
3. Had no contact with travelers in endemic areas or sub-Saharan residents apart from a short half-hour visit to their Malian tenant living in Jardins d'El Menzah.
4. Had not traveled to a malaria endemic area.
5. Went to Turkey a year before his admission with a stay in Antalya for a week.
6. Traveled to Algeria with a one-night stay in Algiers on December 31, 2022, seven months before his hospitalization.
7. Moved with his family to Tabarka (North of Tunisia) three months before his admission.
8. Stayed in Bizerte (North of Tunisia) a month and a half before his admission with suspicion of mosquito bites. The mother traveled to Saudi Arabia four months before her child was hospitalized.

- The conclusions of the epidemiological discussions were:

1. Cases of malaria in Algeria are recorded more in the south of the country and not in Algiers.
2. The trip to Turkey was one year ago while the incubation period of Plasmodium falciparum cannot reach one year.
3. Despite the absence of risk in Mecca (Saudi Arabia), we cannot formally dismiss the hypothesis of a suitcase anopheline.
4. The family lives less than 15 km from the airport, the airport malaria track remains plausible.
5. Further field investigations should be conducted in the regions concerned (Ariana, Tabarka, Bizerte, Tunis Carthage Airport).

- The conclusions of the entomological and epidemiological investigations were:

1. Surveys carried out in Bizerte, Tabarka did not reveal either the presence of Anopheles larvae or Plasmodium vectors due to climate change in recent years and in particular the drought which affects the entire country.
2. No cases of malaria have been recorded around the airport.

DISCUSSION

According to WHO, an indigenous case is one in which local transmission of malaria is confirmed by epidemiological investigation after the exclusion of all other possible sources of infection, including travel to endemic areas, transfusion-related transmission, or airport malaria (1).In this report, all alternative sources were thoroughly investigated and excluded, supporting the hypothesis of a probable indigenous transmission. This unexpected event highlights the importance of maintaining effective surveillance, early diagnosis, and preventive measures to safeguard the malaria-free status of the country

Epidemiological situation

Tunisia has been considered malaria-free since 1979, when the last indigenous case was reported. Since then, nearly all cases have been imported, with about 1,600 cases recorded between 1979 and 2023 according to WHO data (1). Rare "airport malaria" cases have also been documented, including four in 2013 (2–4).

Despite elimination, the risk of re-establishment persists due to vulnerability, receptivity, and susceptibility. Vulnerability is linked to imported cases among travelers, migrant workers, and refugees from endemic regions, with increasing population mobility through Libya and Algeria heightening exposure (2,5). Receptivity depends on the presence of Anopheles labranchiae and Anopheles sergentii, which persist in northern and coastal regions. Vector density shows seasonal peaks during warm, humid months (May–October), favoring parasite development (1,2,5). Although entomological indices suggest low transmission potential, ecological and climatic changes could increase receptivity.

Around twelve post-transfusion malaria cases reported between 1989 and 2016 further emphasize the need for continued vigilance, even in non-endemic areas (3,6). Seasonal fluctuations in vector density, with peaks during the warm and humid months (May–October), may increase the risk of local transmission if parasites are reintroduced. Overall, Tunisia remains susceptible to malaria reintroduction, underscoring the importance of sustained surveillance, early case detection, and proactive vector control measures.

Diagnosis of malaria

Malaria diagnosis in non-endemic areas remains a major clinical challenge, as it relies on clinician suspicion in febrile patients with compatible hematologic or gastrointestinal signs (2,7). In the present case, high parasitemia on blood smear guided the diagnosis, confirmed by rapid diagnostic test (RDT) and thick smear. Hematological abnormalities, including thrombocytopenia and regenerative anemia, are commonly associated with severe malaria (1,2,7).

Parasite confirmation remains essential: microscopy is the gold standard for species identification

and parasitemia quantification, while RDTs provide a practical alternative for non-specialized laboratories. Highly sensitive quantitative PCR can detect submicroscopic infections, which is critical for surveillance (1,2,8,9). Continuous training of laboratory personnel and maintenance of diagnostic capacity are therefore key for malaria control.

Probable origin of the case

Several transmission modes were considered:
1.Imported malaria: This is the most common form since 1979 (2,4). In this case, it was excluded based on the absence of travel to endemic regions; the child and family had only visited Algeria, Turkey, and Saudi Arabia, all malaria-free countries (10).
2. Blood-transmitted malaria: Accidental exposure and post-transfusion malaria were ruled out. Post-transfusion malaria, although documented in Tunisia (3), was excluded as the patient had no recent transfusion history (2).
3. Airport malaria: Rarely, infected Anopheles mosquitoes can be inadvertently transported via aircraft. These so-called "suitcase anophelines" are mosquitoes that survive long-distance travel in luggage or cargo and can bite humans near airports, causing local infections (1,2,4,11). In Tunisia, four such cases were reported in 2013 (4). In our patient, airport malaria is unlikely given the residence 9 km from the airport and the absence of other nearby cases.
4. Autochthonous malaria: Since 1979, Tunisia has not reported local transmission (2). However, local transmission cannot be formally excluded in this case. Factors supporting this hypothesis include the presence of migrant populations from endemic regions, the occasional presence of Anopheles vectors (5,10), and potential ecological receptivity. While entomological investigations detected very low anopheline density, sporadic local transmission may still occur under favorable conditions. Hence, epidemiological surveillance and preventive measures remain critical.

SEVERE MALARIA AND CLINICAL IMPLICATIONS

The case presented with severe Plasmodium falciparum infection, including respiratory distress, severe anemia, and high parasitemia. Severe malaria in young children is associated with increased risk of post-discharge hospitalization and late complications (12). These findings highlight the need for prompt management, including intravenous artesunate followed by oral therapy, and prolonged biological monitoring. The economic and healthcare burden of treating severe malaria in children is also considerable, as reported in recent African studies, where hospital care represents a significant cost to healthcare systems (13). Prevention and early diagnosis remain critical to reduce mortality and morbidity.

IMPLICATIONS FOR SURVEILLANCE AND PUBLIC HEALTH

This case highlights several key points for malaria control and elimination programs:
- Maintaining **continuous epidemiological surveillance** to detect any potential resurgence (1).

- Ensuring clinicians consider malaria in febrile patients, even in non-endemic areas, particularly when hematological and digestive signs are present (2,7).

- Strengthening entomological monitoring to track vector presence, abundance, and ecology (1,5,10).

- Understanding the "suitcase anopheline" phenomenon and airport malaria risk, although rare, is important for preparedness (11).

- Maintaining high laboratory diagnostic capacity through microscopy, RDTs, and PCR when needed (1,2,8,9).

CONCUSION

Although Tunisia has maintained a malaria-free status for over four decades, the occurrence of a probable indigenous case in 2023 demonstrates that eradication does not eliminate risk. Vigilance through surveillance, vector monitoring, and prompt diagnosis is essential to prevent potential re-establishment of malaria transmission.

REFERENCES :

[1] World Health Organization. World malaria report 2023: tracking progress and gaps in the global response to malaria. Geneva: World Health Organization; 2023. Available from: https://iris.who.int/handle/10665/374472

[2] Ministry of Public Health-Tunisia. National guide to malaria management in Tunisia.. 2016. 98 p. http://www.santetunisie.rns.tn/images/anis-doc/gp842016.pdf

[3] Najla F, Kallel A, Ziraoui M, Balloumi D, Ledeb S, Othmane TB, et al. Post transfusion malaria: Current state in Tunisia (new case reported in 2016). Tunis Med. 2019; 97(1): 4-7.

[4] Siala E, Gamara D, Kallel K, Daaboub J, Zouiten F, Houzé S, et al. Airport malaria: Report of four cases in Tunisia. Tunis Med. 2015; 93(8-9): 543-7.

[5] Tabbabi A, Boussés P, Rhim A, Brengues C, Daaboub J, Ben-Alaya-Bouafif N, et al. Larval habitats characterization and species composition of anopheles mosquitoes in Tunisia, with particular attention to anopheles maculipennis complex. Am J Trop Med Hyg. 2015; 92(3): 653-9.

[6] Ben Ammar B, Kallel H, Kallel R, Barsaoui S, Bousnina S, Ben Ammar R. Post-transfusion malaria. Apropos of a case in a child. Tunis Med.1989; 67(2): 101-5.

7] Siala E, Gamara D, Aoun K, Bouratbine A. Malaria

outside a living in endemic areas: diagnosis and measures to take. Tunis Med 2016; 94(6): 167-71.

[8] Siala E, Foudhaili H, Doggi A, Gamara D, Ben Alaya N, Ben Abdallah R, et al. Evaluation and contribution of OptiMAL-IT® test for the diagnosis of imported malaria in Tunisia. Bull la Soc Pathol Exot. 2013; 106(4): 233-8.

[9] Opoku Afriyie S, Addison TK, Gebre Y, et al. Accuracy of diagnosis among clinical malaria patients: comparing microscopy, RDT and highly sensitive qPCR. Malar J. 2023; 22:76.

[10] WHO. International Travel and Health- Country list 18 November 2022 (revised on 3 January 2023). Vol. 2022. 2022. 1-46 p. https://cdn.who.int/media/docs/default-source/travel-and-health/vaccination-requirements-and-who-recommendations-ith-2022-country-list.pdf?sfvrsn=be429f2_4&download=true

[11] Alenou LD, Etang J. Airport malaria in non-endemic areas: New insights into mosquito vectors, case management and major challenges. Microorganisms. 2021; 9 (10): 2160.

[12] Opoka RO, Namazzi R, Datta D, et al. Severe falciparum malaria in young children is associated with an increased risk of post-discharge hospitalization: a prospective cohort study. Malar J. 2024;23:367.

[13] Mori AT, Mallange G, Kühl MJ, et al. Cost of treating severe malaria in children in Africa: a systematic literature review. Malar J. 2024;23:334.